RECLASSIFICATION PETITION MEMO

DATE: September 15, 1999

FROM: John S. Goode, Biomedical Engineer, M.S., John S Goode 9/15/99
Reviewer, Orthopedics Branch
Division of General and Restorative Devices, Mail Code HFZ4 10

THROUGH: Celia Witten, Division Director of General and Restorative Devices
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SUBJECT: Reclassification Petition for Constrained Total Hip Devices

SPONSOR: Orthopedic Surgical Manufacturers Association (OSMA)
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PETITION: Dated: June 1, 1999
AMENDMENTS: Amendment 1 dated: June 8, 1999
Amendment 2 was not dated by the sponsor but was received by FDA on August 27, 1999. (Note: Amendment 2 contains the Original June 1, 1999 Petition, and Amendments 1 and 2. Therefore, Amendment 2 (2 Volumes) is the only document sent to the panel.)

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APPENDICIES

ADMINISTRATIVE:

The petition was submitted under Section 515(i) (21 USC 360e (i)), with specific reference to FDA's 515(i) Order of August 14, 1995, which required the submission of safety and effectiveness information on certain Class III devices, among which was Constrained Metal/Polymer Hip Prostheses.

SECTION 1 OF THE PETITION: INTRODUCTION

OSMA submitted a petition for reclassification of a constrained Metal/Polymer Hip Prosthesis, Cemented or Uncemented, from Class III to Class 11. The sponsor stated that both the semi-constrained total hip joint replacement prostheses (Class II) and the constrained total hip joint replacement prostheses are used for similar general indications and bear similar risks. The only significant difference between the semi-constrained and constrained devices is the degree of constraint of the polymer acetabular liner. The constrained liner retains the ball of the femoral component to stabilize the joint and resist dislocation. It is used to treat patients at high risk of hip dislocation due to a history of prior dislocation, bone loss, soft tissue laxity, intra-operative instability, and/or neuromuscular disease. The semi-constrained liner relies on the soft tissue in the hip joint to stabilize the joint.

The sponsor stated that since the FDA classified these devices into Class III, the development of devices and surgical technique has continued and a considerable quantity of published clinical results have appeared in the peer-reviewed literature. This body of "new information" provides the grounds for the present petition. The sponsor believes that the presently-existing clinical literature provides sufficient safety and efficacy information to adequately define the risks associated with the device, and that FDA's statutory authority under Labeling, Pre-Market Notification, GMP, and Special Controls are sufficient to ensure the safety and effectiveness of constrained hip prostheses as class II devices.

SECTION II OF THE PETITION: PROPOSED INTENDED USE

The constrained acetabular cup is indicated for use as a component of a total hip prosthesis in patients at high risk of hip dislocation due to a history of prior dislocation, bone loss, soft tissue laxity, neuromuscular disease, or intra-operative instability.

SECTION V OF THE PETITION: BASIS FOR PETITION

The sponsor stated that this petition seeks reclassification of Constrained Metal/Polymer Hip Prostheses from class III to class II. The sponsor stated that long term data now exists that addresses the risks that originally led to placement of these devices into class III. The sponsor stated that the published results show consistency in pain relief, restoration of function, and reduction in recurrence of dislocation.

SECTION IV OF THE PETITION: REGULATORY HISTORY OF DEVICE

Constrained Metal/Polymer Hip Prostheses (21 CFR 888.3310) are pre-amendments Class III devices. On July 2, 1982, after reviewing the recommendations of the Orthopedic Device Section of the Surgical and Rehabilitation Devices Panel, the FDA issued a proposed rule (47 FR 29052) classifying 77 orthopedic devices. Constrained hip devices were proposed for class III.

The July 2, 1982 proposed rule for Constrained Hip Prostheses included the following comments:

- The panel recommended a classification in Class III and that premarket approval of this device be a low priority.
- The following general risks to health included: infection, thromboemboli generation, corrosion of metal implants, re-operation, complications due to use of bone cement and metal alloys.
- Summary of reasons for recommendation:
  - These devices are implanted and intended to be used in relieving disabling pain and in restoring or minimizing further loss of functional use of a joint or limb. The panel believed these uses to be of substantial importance in preventing impairment of human health.
  - The panel believed that general controls alone would not provide sufficient control over these characteristics. The panel also believed that it is not possible to establish an adequate performance standard for the device. There is a lack of safety and effectiveness data to demonstrate the satisfactory performance of the device. The panel found insufficient information exists to support the conclusion that general controls or performance standards will be adequate to provide reasonable assurance of the safety and effectiveness of the device. Therefore, the device must be subject to premarket approval to assure its safety and effectiveness.
  - Data on which the recommendation was based: panel member's personal knowledge of, and clinical experience with, the device.
  - Risks to health included:
    - Loss or reduction of joint function:
      - Improper design or inadequate mechanical properties of the device such as, its lack of strength and resistance to wear, may result in a loss or reduction of joint function due to excessive wear, fracture, deformation of the device, or loosening of the device from the surgical cavity;
    - Adverse tissue reaction (biological and mechanical); and
    - Infection.
  - FDA agreed with the panel recommendations.

The final rule classifying orthopedic devices was published September 4, 1987 (52 FR 33686). This formally established constrained hip devices as pre-amendment class III devices.

On September 4, 1987, FDA published the final rule classifying constrained hip prostheses in Class III.

- Summary of comments received and printed in the Sept. 4, 1987 Federal Register:
  - A comment argued that this device should not be classified because it is no longer commercially distributed. FDA agreed that the device was not currently commercially distributed but was commercially distributed before the enactment date of the amendments. Therefore, in the final rule, FDA adopted the proposed regulation for constrained liners as Class III devices.

From September 4, 1987 to December 26, 1996, manufacturers were able to market constrained hip devices via 510(k) notifications that the FDA determined to be substantially equivalent to pre-amendments predicate devices. On September 7, 1995, FDA published a proposed rule (60 FR 46718) to require the filing under section 515(b) of the act of a PMA or notice of completion of a PDP for 43 class III medical devices. Included in this list was constrained metal/polymer hip prostheses. The comment period closed on January 5, 1996 and according to the FDA Dockets Management Branch, Docket 95N-0084 received no new comments regarding constrained hip prostheses. On September 27, 1996, the final rule was published (F61FR50704) for 41 of the 43 class III devices, requiring PMAs or PDPs by December 26, 1996. Two orthopedic companies, Johnson & Johnson and Osteonics, filed PMAs for the constrained hip prostheses and both PMAs were approved in June 1997.

CLASSIFICATION QUESTIONNAIRE:

The sponsor provided a completed classification questionnaire on pp.!-2.

SECTION II OF THE PETITION: PROPOSED DEVICE DESCRIPTION

Total hip prostheses generally consist of two components, a femoral component and an acetabular component. Either of these components can be modular in design (e.g., a taper-fit femoral head, and a metal acetabular shell with polymer liner). The femoral component is intended to replace the femoral head, and its stem is inserted into the intramedullary canal of the femur to anchor it. Femoral components are made of alloys such as cobalt-chromium-molybdenum or titanium alloys. Femoral components may be fabricated as a single piece (head-stem) or it may be modular (with separate head and stem components) with a selection of head diameters/neck lengths that can be fitted to a stem of a chosen size. Modular components are generally fitted together by Morse taper connections. Femoral stems may be cemented or press-fit into the intramedullary canal. The spherical femoral head is designed to articulate with the acetabular component that is fixed into the prepared acetabulum. The constrained acetabular component generally consists of a metal she!! made from cobalt-chromium-molybdenum or titanium alloys assembled with a constrained polymer liner fabricated from ultra-high-molecular-weight polyethylene (UHMWPE). The metal shells come in various styles and sizes to fit the anatomy. Acetabular components are fixed with bone cement, bone screws, and/or porous coating.

The constrained liner retains the ball of the femoral component to stabilize the joint and resist dislocation. The sponsor stated that this reduces the travel-distance of the femoral neck and the range of motion. The constrained acetabular component generally consists of a metal she!! made from CoCrMo or Ti alloys assembled with a constrained polymer liner made from UHMWPE. The metal shells come in various styles and sizes to tit the anatomy. Acetabular components are fixed with bone cement, bone screws, and/or porous coating. If bone cement is not used to affix the constrained acetabular component, a supplemental method of fixation, in addition to press fitting, is recommended to assure initial stability (e.g., bone screws, spikes, screw threads, fins, etc.).

SECTION VI AND VIII OF THE PETITION: PROPOSED PRE-CLINICAL TESTS

The sponsor identified five potential failure modes for the constrained liner. The snonsor then conducted testing to establish one of me device's (Biomet Ringloc Constrained Hip Device) resistance to five potential failure modes. The tests the sponsor performed to address the failure modes are just examples of possible tests which may address the potential failure modes. The five failure modes were:

- Liner Loosening from a well-fixed Acetabular Shell: Liner Push Out and Lever Out.
- Femoral Head Dislocation from the Liner: Pull-out and Lever-Out.
- Insufficient Area for Stress Transfer between the Liner and the Metal She!!: Cup/Liner Conformity.
- Inability to Assemble the Components at the Time of Surgery: Push-in.
- Wearing Out of the Liner Due to Repeated Articulations During the Gait Cycle.
- In addition, the sponsor would characterize the UHMWPE and other materials used to fabricate the device components.

SECTIONS II AND VI OF THE PETITION: CLINICAL STUDIES

Control - Semi-Constrained Total Hip Clinical Studies:

The sponsor summarized 9 published articles that had reported on 23,73 1 cases to establish a historical dislocation rate of 3.3% (range: 1-6%) following total hip replacement. The sponsor stated that the literature search was conducted in the MEDLINE database using, "dislocation, hip" as the search word combination and the nine articles covering the largest number of cases were chosen. The sponsor listed the authors of the articles and the corresponding dislocation rates on p.6.

In Section IV, the sponsor summarized three of the semi-constrained total hip clinical studies. The three studies were written by:

- #7 Schulte, KR, et al., "The outcome of Charnley total hip arthroplasty with cement after a minimum twenty-year follow-up. The results of one surgeon." JBJS 1993, July 75(7): 1418.
- #8 Turner, RS, "Post-operative total hip prosthetic femoral head dislocations incidence, etiologic factors, and management." Clinical Orthopaedics, 1994, April (301): 196-204.
- #6 Patemo, SA, et a!., "The influence of patient related factors and the position of the acetabular component on the rate of dislocation after total hip replacement." JBJS Vo! 79-A, No 8, August 1997.

These three studies were summarized as follows:

Study	Schulte (#7)	Turner (#8)	Patemo (#6)
Device	Semi-Constrained	Semi-Constrained	Semi-Constrained
Number of Cases	322	561	446
Sex	159 male: 171 female	2 15 male; 346 female	208 male; 349 female
Type of Surgery	254 primary; 68 revision	477 primary; 84 revision	39 1 primary; 169 revision
Follow-Up	20 year minimum	2-20 years	Primary 6 yr.avg. (range 2-12yrs.); Revision 5 yr.avg. (range 2-10yrs.)
Dislocations following Surgery	3/322 (1%); 1/98 (1%) alive at 20 years post-op	25/561 (4.5%); 9/25 recurrent	32/560 (6%); 17/391 (4%) for primary; 15/169 (9%). revision
Evaluation at most recent follow-up	Outcome at 20+ years: 83 (85%) no revision; 9 (9%) 1 revision; 4 (4%) 2+ revision; 2 (2%) resection	Not reported	Study found no effects of age, gender, obesity, or diagnosis on dislocation after primary or revision
Time to Dislocation	Not reported	Range: 1-9yrs.	Avg. 4 mo. (range 0-38mo.); 7 occurred in hospital
Acetabulum Radiographically Stable	2791322 (87%)	Not reported	Not reported
Pain Function Deformity ROM	90% none to mild 78% walk 30min-no limit 98% no aid-use cane N/A	Dislocation rates only	Dislocation rates only

Constrained Total Hip Clinical Studies:

The sponsor provided 5 published series for **the J&J S-ROM Poly-Dial Constrained Acetabular Liner:**

- Lombardi, et a!., 1991, reported on 55 patients receiving 57 constrained devices. The average follow-up was 28 months (range 24-35 months). The sponsor provided average (69) and range (39-91) of ages, sex (30 female), indications and primary diagnoses. There were 6 primary, 5 1 revision patients.

The sponsor provided the following results:

Safety	Efficacy		
5 of 55 patients re-dislocated a total of 8 times in an average time of 2.5 months	HHS	PreOp	PostOp (avg.30mo.)
The author's historical dislocation rate in 176 revision THR was 19%, but lowered to 4.5% using constrained hip.	Total	36.3	67.3 (range:29-94)
Dislocation at 1 month, modified neck length and cup angle	Pain	19.6	37.2
Dislocation at 2 months, ring disengaged	Function	13.9	23.5
Dislocation at 1 and 2 months, Parkinsonism			
2 dislocations at 1 and 9 months, insert rotated, wear and dislocation	Deformity	0.1	3.2
2 dislocations at 2 and 3 months, adductor tenotomy, girdlestoned infection from decubitous ulcer	ROM	2.7	3.4

The outcomes were compared to a non-randomized, concurrent series of 155 patients in physician's own practice who underwent 176 revision total hip arthroplasties not using the S-ROM Poly-Dial Constrained Acetabular Liner. The dislocation rate for the control group was 19%.

- Anderson, et a!., 1994, reported on 2 1 consecutive cases. The average follow-up was 3 1 months (range 24-64 months). The sponsor provided dates of study, average and range of ages, sex, indications and primary diagnoses. Eighteen were chronic dislocators and 3 were intra-operative instability. The sponsor provided the following results:

Safety	Efficacy	
3 infection, 1 implant malposition	HHS Excellent	7 patients
1 implant failure	HHS Good	2 patients
8 dislocations in 6 patients (29%). Average time to dislocation was 10 months	HHS Fair	2 patients
15 patients (71%) experienced no subsequent dislocation	HHS Poor	10 patients
No acetabular migration seen in any patient; 3 of 19 with porous ingrowth acetabular components developed evidence of lucent lines (with no progression)	(6 dislocations, 2 lower back pain (no hip pain), 2 had multiple revisions)	
No radiographic or clinical evidence of loosening in the 19 porous ingrowth acetabular components was observed.	Final HHS 76 (range: 32-100)	
Adverse events also included 1 deep sepsis and 1 peroneal nerve palsy	Post-op ROM average 102° flex/ext; (range 45°-140°)	

For those patients who redislocated (n=6), an increased acetabular abduction angle of the metallic acetabular cup, averaging 70°, was the only predictive factor of failure of the constrained cup ($p<0.05$). In these 6 patients, there were 8 dislocations. Four dislocations involved pulling the UHMWPE liner from the metal cup; 2 dislocations involved the femoral head becoming disengaged from the liner itself; and 2 dislocations occurred after the metal reinforcing ring had become disengaged from the neck of the UMMWPE liner. Significant trauma was the mechanism for failure of the constrained device in only one patient. The remaining 5 patients a!! suffered dislocations while engaged in everyday activities.

- Cameron, 199 1, reported on 1 of 6 revision cases performed over 4 years. Patient dislocated with semi-constrained device and received constrained socket. At 2 years follow-up, hip is stable and pain free. Patient wore hip abduction brace for 6months post-operatively.
- Fisher, et a!., 1994, reported on 2 cases. Both patients received constrained hips for dislocation with semi-constrained devices. Subsequently, both cases fell down stairs causing dislocation and requiring cup revision with another constrained hip. At 18 months follow-up, one ambulatory with walker, one with cane. Radiographically, no evidence of separation. Note from author: 5/5 1 patients have suffered an additional dislocation or disassociation after receiving a constrained liner.
- Kaper, et al., 19890996, reported on 2 of 4 cases. One received a constrained liner after repeated dislocations with semi-constrained device, asymptomatic at latest follow-up. Other patient received a constrained liner after repeated dislocations with semi-constrained device, followed by dislocation and open reduction. Author reports 2 failures due to fracture of constraining ring and 2 revisions due to dislocation of femoral head from the constrained socket.

The sponsor provided 2 published series for the **Osteonics Omnifit Constrained Acetabular Liner:**

- Goetz, et a!., 1988-1993, reported on 55 patients receiving 56 constrained hips. The average follow-up was 64 months (range 37-97months). The author reported the dates of surgery, average and age range, sex, operative hip, indications and primary diagnoses. The sponsor reported the following data:

Safety	Efficacy		
1 (3%) Recurrent Dislocation	Pain	Function	Walking Aids
5 (13%) Reoperation • 2 infection • 1 allograft failure • 1 periprosthetic fracture • 1 aseptic cup loosening	**28 (72%) No** Pain	19 No Limp	12 No Support
10 trochanteric nonunion	7 (18%) Mild Pain	12 Mild Limp	14 Cane
2 intraoperative fractures	3 (8%) Moderate Pain	6 Moderate I Limo	11 Crutches/ Walker
1 deep venous thrombosis			
1 incomplete sciatic nerve palsy	1 (3%) Severe Pain	2 Unable to Walk	2 Wheelchair
1 severe heterotopic ossification			

- Goetz, et a!., 1988-1993, reported on 98 patients receiving 101 constrained hips. The average follow-up was: (Group 1) 61months (range 24-97months) on 74 living patients (77 hips) and (Group 2) 1 9months (range l-8 1 months) for 23 deceased patients. The author reported the dates of surgery, average (7 1) and age range (3 1-92), sex (65 females), operative hip (54 right), indications and primary diagnoses. Fifty-six recurrent dislocation and 38 intra-operative instability. The sponsor reported the following data:

Safety	Efficacy		
2/23 (9%) dislocation group 1 2/77 (3%) dislocation group 2	Pain	Function	Walking Aids
	68 No Pain	35 No Limp	23 No Support
2/23 (9%) re-operation group 1 10/77 (13%) re-operation group 2	16 Mild Pain	35 Mild Limp	29 Cane
Long list of other complications including: trochanteric nonunion, intra-operative fracture, etc.	8 Moderate Pain	16 Moderate Limp	35 Crutches/ Walker
	4 Severe Pain	11 Severe or Unable to Walk	10 Wheelchair

Finally, the sponsor provided information on the **Biomet Ringloc Constrained Hip.**
Combining al! of the information together, Groups 1 and 2 (patients implanted before the call for PMA and patients implanted after call for PMA, respectively), the sponsor provided the following information:

- The total number of patients implanted was 154. Sponsor provides average and age ranges, average weight and weight ranges, and sex.
- The sponsor reported the mean Pre-Op HHS to be 46.6 (range 10-94). Note: We don't know how many patients were averaged for this score.
- 9 patients had recurrent dislocation. 1 had radiolucent lines. 1 was loosening. 98 were stable.
- 14 patients had liner revisions, 9 other revisions, and 7 infections.
- The average post-Op HHS was reported to be 70 (n=45 patients; range O-100).
- The sponsor provided a list of complications reported. The most prevalent were revision, recurrent dislocation, infection, and aseptic loosening.

AMENDMENT 1: SUMMARY OF CONSTRAINED COMPONENT FIXATION METHODS

Number of Cemented and Uncemented Procedures from the Reference Literature Articles

J&J and Osteonics	Acetabular Cups		Femoral Stems	
Devices	Cemented	Uncemented	Cemented	Uncemented
Reference: #10	2	19	<21 Undetermined>	
Reference: #11	-	1	<1 Undetermined>	
Reference: #12	-	2	1	1
Reference: #13	-	36	33	5
Reference: #14	12	89	92	9
Reference: #15	-	2	-	2
Reference: #16	-	57	<57 Undetermined>	
Reference: #17	-	1	-	1
Reference: #18	1	-	1	-
Total:	15	207	127	18

Biomet Ringloc Study				
	Acetabular Cups		Femoral Stems	
	Cemented	Uncemented	Cemented	Uncemented
Total:	22	60	37	33
	<72 Undetermined>		<84 Undetermined>	

SECTION III: CFR CLASSIFICATION (CURRENT AND PROPOSED)

The sponsor provided the current CFR Identification and Classification for Constrained Hip Prostheses (888.33 10) and proposed the following modifications:

Current:

888.33 10 Hip Joint Metal/Polymer Constrained Cemented or Uncemented Prosthesis:

(a) Identification

A hip joint metal/polymer constrained cemented or uncemented prosthesis is a device intended to be implanted to replace a hip joint. The device prevents dislocation in more than one anatomic plane and has components that are linked together. This generic type of device includes prostheses that have a femoral component made of alloys such as cobalt-chromium-molybdenum, and a acetabular component made of ultra-high-molecular-weight polyethylene with or without a metal shell made of alloys such as cobalt-chromium-molybdenum and titanium alloys. This generic type of device is intended for use with or without bone cement (888.3027). This device is not intended for biological fixation.

(a) Classification

Class II

888.33 10 Hip Joint Metal/Polymer Constrained Cemented or Uncemented Prosthesis:

(b) Identification

A hip joint metal/polymer constrained cemented or uncemented prosthesis is a device intended to be implanted to replace a hip joint. The device prevents dislocation in more than one anatomic plane and has components that. are linked together. This generic type of device includes prostheses that have a femoral component made of alloys such as cobalt-chromium-molybdenum, and a acetabular component made of ultra-high-molecular-weight polyethylene with **or without a metal shell made of alloys such as cobalt-chromium-molybdenum and titanium alloys.** This generic type of device is intended for use with or without bone cement (888.3027). (Note: **Removed sentence: This device is not intended for biological fixation.)**

(c) Classification

Class II

The device description was expanded to include metal shells. (Note: the original classification just mentioned PE acetabular components). In addition, the last sentence in the original identification has been removed. (Note: the original classification excluded devices fixed through biological fixation).

SECTION VII: MEDICAL DEVICE REPORTS

The sponsor searched the medical device reports and found a total of 68 MDRs that contained 9 1 adverse events from 7 manufacturers. Sixty-three (63) reports (86 events) involved serious injury and five (5) reports (5 events) were malfunctions.

\Company Event\	Biomet *(since 5/95, 900 sold)*	Exactech	DePuy	Zimmer	Osteonics (4/89-11/96 1224 sold)	J&J (9/91-3/97 5468 sold)	Joint Med.	**Total**
Dislocation#	6	1	1	1	1	23	23	**56**
Disengaged Liner#	3				6	2		**11**
Ring Broken#	1					5	1	**7**
Ring Migration#					1		1	**2**
Revision#	1			1			3	**5**
Cement Loosening#					1			**1**
Broken Insert (Implant)#	1						1	**2**
Tapers Unlocked#						1		**1**
Liner Wear#						1		**1**
Size Mislabled*			1					**1**
Device Split*							1	**1**
Poor Liner Fit*						1	1	**2**
Ring Wouldn't Fit*							1	**1**
Total	**12**	**1**	**2**	**2**	**9**	**33**	**32**	**91**

Sponsor categorized these events as serious injuries.
* Sponsor categorized these events as malfunctions.

The sponsor provided the following additional information regarding dislocation in the MDRs:

There were 56 events that were considered dislocations.

- 25 were of unknown cause;
- 12 occurred during normal activities (chair, toilet, turning in bed);
- 10 occurred from lever-out (impingement on acetabular rim); and
- 9 were due to misalignment (mixing components from different manufacturers, using skirted head/neck, improper placement angles).

There were 15 events that were listed separately from dislocations due to broken components, patient falls, or other extenuating circumstances.

- 10 dislocations were subsequent to broken components (10 locking rings);
- 4 dislocations/disassociation were attributed to falls; and
- 1 dislocation occurred subsequent to tissue loss from a gunshot.

SECTION VIII: REGULATORY CONTROL OF RISKS

The sponsor proposed the following regulatory control of risks. Device risks can be handled through material standards, with substantial equivalence determinations serving to control device design. Patient and surgical risks can be minimized through device labeling, and device quality through GMP. FDA **has** authority through the 5 1 O(k) process, as well as its general authority over misbranding and adulteration to impose controls along these lines. Additionally, guidance documents are commonly used and provide vehicles for specific provisions regarding materials, testing, and labeling. The sponsor identified the following potential risks and means to control or minimize the risks:

Risks/Complications **Identified in this Petition**	**Means to Control/Minimize Risks**
Infection	1.5 1 O(k) Requirement – Sterility Adulteration Authority – GMP Sterility Misbranding Authority – **Labeling** Indications/Contraindications/Warnings/Precautions
Loosening of Components	510(k) Requirement – SE **Design** Misbranding Authority – **Labeling** Precautions/ Warnings
Revision of Components Dislocation of the Hip Prosthesis	510(k) Requirement – SE **Design** 5 10(k) Requirement – **Pre-Clinical Testing** Femoral head pull-out/acetabular insert dislocation 5 I O(k) Requirement – **Conformance to Material Standards** Misbranding Authority – **Labeling** Precautions/warnings
Implant Failure/Fracture/Wear Osteolysis Sensitivity to Implant Materials	5 1 O(k) Requirement – SE **Design** 5 10(k) Requirement – **Conformance to Material Standards** 5 10(k) Requirement – Pre-clinical **Testing** Femoral head pull-out/wear/acetabular insert dislocation/ FDA guidance documents Adulteration Authority – GMP Manufacturing and Design
Nerve Impingement/ Damage Pain Vascular Disorders Pulmonary Embolism Gastrointestinal/Genitourinary Complications	Misbranding Authority – **Labeling** Warnings/ Precautions

Note: Bolded items include special controls

In addition to the items above, the sponsor identified IO voluntary standards from the American Society for Testing and Materials (ASTM), and 6 FDA guidance documents as specific special controls to reasonable assure the safety and effectiveness of the constrained metal/polymer hip prosthesis.

ASTM Standards:

- ASTM F67 Standard Specification for Unalloyed Titanium for Surgical Implant Applications;
- ASTM F75 Standard Specification for Cast Cobalt-Chromium-Molybdenum Alloy for Surgical Implant Applications;
- ASTM F136 Standard Specification for Wrought Titanium-6 Aluminum-4 Vanadium ELI (Extra Low Interstitial) Alloy for Surgical Implant Applications;
- ASTM F648 Standard Specification for Ultra-High-Molecular-Weight Polyethylene Powder and Fabricated Form for Surgical Implants;
- ASTM F 1044 Standard Test Method for Shear Testing of Porous Metal Coatings;
- ASTM F1147 Standard Test Method for Tension Testing of Porous Metal Coatings;

- ASTM F 1377 Standard Specification for Cobalt-28 Chromum-6 Molybdenum Powder for Coating of Orthopedic Implants;
- ASTM F1580 Standard Specification for Titanium and Titanium-6% Aluminum4% Vanadium Alloy Powders for Coating of Surgical Implants;
- ASTM F1814 Standard Guide for Evaluating Modular Hip and Knee Joint Components;
- ASTM F1820 Standard Test Method for Determining the Axial Disassembly Force of a Modular Acetabular Device.

FDA Guidance Documents:

- Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Aposing Bone or Bone Cement;
- Guidance Document for Testing Non-Articulating, "Mechanically Locked" Modular Implant Components;
- Draft Guidance Document for the Preparation of Premarket Notification 5 1 O(k) Applications for Orthopedic Devices - The Basic Elements;
- Data Requirements for Ultra-High-Molecular-Weight Polyethylene (UHMWPE) Used in Orthopedic Devices;
- Use of International Standard ISO – 10993, Biological Evaluation of Medical Devices Part I: Evaluation and Testing;
- 5 1 O(k) Sterility Review Guidance and Revisions of 1 1/18/94 and ORDB 7/3/97 (K90-1)

SECTION IX: DEVICES CURRENTLY/PREVIOUSLY AVAILABLE

The sponsor stated that polymer liners are not interchangeable from manufacturer to manufacturer. Therefore, in the interest of public health, the manufacturer of the prosthesis must be allowed to provide a constrained liner that tits into that specific acetabular shell.

Currently Available Constrained Acetabular Cups:
Since December 1996, there have been only two constrained acetabular components approved for marketing in the United States:

1. Osteonics, Constrained Acetabular Insert, P960047: Approved on June 13, 1997
2. Johnson and Johnson Professional, Inc., S-ROM Poly-Dial Constrained Liner, P960054: Approved on June 19, 1997.

Previously Available Constrained Acetabular Cups:
Before December 1996, several constrained hip liners were commercially available. Some of these devices were cleared via the 510(k) process, and others may have been provided "on demand" to physicians as "customized" devices to treat patients with chronic dislocation.

1. Cleared Devices 510(k):
   - K950202: Biomet Ringloc Constrained Liner, cleared 5/15/95
   - K870088: Joint Medical S-ROM Supercup Acetabular Cup, cleared 4/22/88
   - K803 192: Osteonics Corp., HCL Acetabular Components, cleared 1/23/81

2. Devices that may have been provided for specific patients (custom use):
   In searching the MDR and device listing databases, the sponsor found at least 5 additional manufacturers provided constrained acetabular cups since the mid-1980s.

FINANCIAL DISCLOSURE:

The sponsor stated that they do not believe the financial disclosure by clinical investigators is applicable to this submission for the following reasons:

- All cases and follow-up evaluations were completed prior to February 2, 1999;
- The subjects were patients treated during the physicians' normal course of practice, and were not research subjects;
- The retrospective collection of clinical data involving a commercially marketed device does not meet the definition of a covered clinical trial.

APPENDIX 1: GENERAL LABELING INFORMATION

In Appendix 1, the sponsor provided general labeling for constrained liners including indications for use, device description, contraindications, warnings, precautions, potential adverse effects, sterility and handling.

APPENDIX – 1

GENERAL LABELING INFORMATION

I. Indication for Use.

The metal/polymer constrained acetabular liner is indicated for use as a component of a total hip prosthesis in primary and revision patients at high risk of hip dislocation due to a history of prior dislocation, bone loss, joint or soft tissue laxity, neuromuscular disease, or intraoperative instability.

II. Device Description.

The constrained metal/polymer acetabular insert is part of a prosthetic hip joint made of metal such as titanium alloy or cobalt-chromium-molybdenum alloy and ultra-high molecular-weight polyethylene (UHMWPE). The device utilizes a total hip prosthesis head that is captured within an outer UHMWPE acetabular insert with a metal shell. The bipolar type version of the constrained liner generally consists of a femoral head that is captured within a larger polyethylene lit- ' .ead ' ch that there is articulation both at the head-to-bipolar interface and at the bipolar-to-outer cup interface. The traditional bipolar assembly is itself captured by an outer polyethylene liner that, in turn is assembled to a standard acetabular shell.

In both styles, the spherical head of the femoral stem is restrained within the acetabular cup device, usually by an UHMWPE ring.

III. Containdications, Warnings. Precautions, and Potential Adverse Effects.

1. Relative Contraindications

a. Bone or musculature compromised by disease, infection, or prior implantation that cannot provide adequate support or fixation for the prosthesis.

b. Any active or suspected infection in or about the hip joint

c. Skeletal immaturity

2. Warnings

a. Closed reduction of a dislocation of a constrained hip prosthesis is not possible. Patients should be made aware that treatment of device dislocation would require additional surgery.

b. Patients should be warned on the impact of excessive loading that can result if the patient is involved in an occupation or activity that includes substantial walking, running, lifting, or excessive muscle loading due to patient weight

causing extreme demands on the constrained insert can result in the failure of the device. Extreme demands on the device may also cause loosening of the acctabular shell.

C. Alteration of any factory pre-assembled components can result in improper function of the retaining mechanisms, and failure of the device. Discard or return any constrained insert if the retaining mechanism appears damaged or mishandled.

d. Improper alignment of the acetabular insert within the acetabular shell prior to impaction may result in damage to the locking mechanism, or improper seating of the constrained acetabular insert.

e. Bending, contouring, or modifying this device may adversely affect the implant potentially leading to early implant failure.

f. Do not use steam autoclaving for resterilization of the UHMWPE liner, as it may result in serious deformation and material deterioration.

g. Do not combine components from different manufacturers. This may lead to premature wear or failure of the device.

3. Precautions

a. Careful selection of components and familiarity with all aspects of the surgical technique are important to the success of the surgery.

b. An implant should be handles carefully to avoid damage that could compromise the mechanical integrity of the device and cause early failure or loosening.

C. Inspect implants for nicks, scratches, or other defects that may cause failure of the implant.

d. To prevent contamination of the prosthesis, keep free of lint and powders. Do not open the package until surgery. Do not place the implant in contact with prepared bone surfaces before the final decision to implant has been made.

e. An implant should never be reused. Any implant once assembled and Disassembled should be discarded. Even though it appears undamaged, it may have small defects and internal stress patterns that may lead to failure.

f. The wear rate of prosthetic contact surfaces is greatly accelerated if loose

fragments of bone cement become detached and act as an abrasive in the bearing surfaces. When using bone cement, care should be taken to remove all excess cement from the periphery of the implant.

g. If a metal acetabular shell is affixed without bone cement, an additional method of initial fixation (e.g. bone screws, spikes, screw threads, fins, etc.) should be utilized to assure early stabilization of the cup.

4. Potential Adverse Effects

a. Infection

b. Pain

C. Loosening, wear, or mechanical failure of the prosthetic components

d. Dislocation of the hip prosthesis requiring additional surgery

e. Localized progressive bone resorptio (osteolysis)

f. Nerve impingement or damage, vascular disorders (including thrombus)

g. Heterotopic bone formation

h. Sensitivity to implant materials

i. Gastrointestinal and/or genitourinary complications

j. Pulmonary embolism

k. Death

l. Myocardial infarction

IV. Sterility and Handling

1. Acetabular components are supplied pre-sterilized by a minimum of 25 kGy of gamma irradiation.

2. Do Not Re-Sterilize - For Single Use Only

3. Components are sterile unless the package is damaged or opened. Use by date - if applicable.

4. CAUTION: FEDERAL (USA) LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN.

APPENDIX 2: BIBLIOGRAPHY/COPIES OF PUBLISHED ARTICLES

In Appendix 2, the sponsor provided a bibliography of found articles regarding dislocation rate and constrained hip replacement. The sponsor provided summaries and copies of these 16 articles on pp. 172-317.

Supplement Dated June 9, 1999:

In a supplement dated 6/9/99, the sponsor identified the search engines and criteria used for the bibliography; revised bibliography and copies of two additional articles; and provided a summary of cemented/uncemented cases and device types (where available).

The sponsor stated that the literature search was done using WWW.ORTHOGUIDE. COM that includes a Medline Search designed for orthopedics. Further clarification of the search criteria was provided.

APPENDIX 2

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A. Dislocation Rate

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